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09/242,343	04/12/1999	DIRK VOLLENBROICH	2694-119P	9955

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	28

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/242,343	VOLLENBROICH ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-15 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-15 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. This action is in response to the RCE filed on February 5, 2003, which in turn was in Response to the Final action (now the prior action) mailed on January 4, 2002. The claims currently pending, and under consideration, in the application are claims 1-11, 13-15, and 18. In the RCE, claims 1,2, and 18 were amended; and claim 19, which was rejected in the prior action, was cancelled.

2. The Art Unit location of your application, and the examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

Claim Objections

3. **(New Objection)** Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This claim depends from claim 1, which describes a method of reducing viral titer in a sample by contacting it with a lipoheptapeptide at room temperature for a period of between 30 minutes to an hour. For the purposes of this objection, Claim 2 is read as further limiting the method of claim 1 such that the product is

contacted at temperatures "higher than room temperature" for a "period of 5-30 min." Each of the ranges provided by claim 2 are outside the scope of the invention as defined by claim 1. As such, this claim is not properly dependant on claim 1.

4. **(New Objection-Necessitated by Amendment)** Claim 3 is objected to because of the following informalities: it is suggested that the applicant clarify that "a chemically synthesized lipopeptide" is a separate choice from "a lipopeptide produced or modified by genetic engineering" by inserting a comma between the phrases "synthesized lipopeptide" and "or a lipopeptide produced..." Appropriate correction is required.

5. **(New Objection)** Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This claim depends from claim 1, which describes the use of a lipopeptide according to formula I. While claim 4 restates the boundaries of formula I, it does not appear to add any further limitations thereto.

6. **(New Objection-Necessitated by Amendment)** Claim 18 is objected to because of the following informalities: in line 2, the claim refers to "biotechnologically produced product product." Appropriate correction is required. It is suggested that the second "product" be deleted.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior Rejection- Withdrawn)** Claims 1-9, 13-15, 18, and 19 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims were rejected because no units were assigned to the measurement of the claimed decrease in viral infectivity. In view of the Applicant's arguments presented in the response filed on June 4, 2002, the rejection is withdrawn.

9. **(New Rejection)** Claims 1-11, and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. . The Applicant has amended these claims to read on methods of rendering "a purified product isolated from blood or a biotechnologically produced product substantially free of lipid enveloped viruses." It is unclear what is encompassed by this term as the applicant argues that the claims read on cell-free products, but the specification does not exclude cellular products from the definitions of these terms. However, it is noted that there are several examples provided as to the types of products that may be rendered substantially virus free by the claimed method. See, App., pages 2 and 9. Most of these products are specific proteins, but the application also lists recombinant and human proteins generally. In view of this, it is suggested that the claims be amended to read on the rendering of

isolated proteins, rather than blood or biotechnologically produced products, substantially free of virus.

10. **(New Rejection)** Claims 1-11, and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on methods of rendering products substantially free of lipid-enveloped viruses "by a factor of approximately $>10^4$." This terminology is rejected as indefinite for two reasons. First, the applicant is in essence claiming a factor that is approximately greater than 10^4. It is unclear what is meant by approximately greater than a number.

Secondly, because the claim includes this phrase, but does not include a limitation that requires that the isolated product being treated has a virus titer of greater than 10^4, the claim is internally inconsistent. For example, if the sample being treated has a starting viral titer of 10^4 or less, according to the applicant's claim, the result would be a composition with a negative viral titer. As such cannot be the case, the claim is rejected as unclear because it is internally inconsistent.

11. **(New Rejection)** Claims 4-8, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 is representative of these claims. This claim purports to further limit claim 1 by identifying the lipoheptapeptide of formula 1. In the claim, it is unclear in the claim what is meant by the phrase "are used as lipopeptides" is intended to

convey. It is also unclear how the phrase "in which formula I," relates to the rest of the claim. As the claim does not appear to be further limiting claim 1, it is suggested that claim 4 be cancelled, and the dependant claims be amended to depend from claim 1.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. **(Prior Rejection-Maintained)** Claims 1-10, 13-15, 18, and 19 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vitro inactivation of lipid-enveloped viruses, does not reasonably provide enablement for in vivo inactivation. As claim 19 has been cancelled from the application, the rejection is withdrawn as to this claim as moot. The Applicant's arguments that the claims read on methods of reducing titer, and not of products is found persuasive. However, the Examiner does not entirely agree with the applicant's arguments regarding that the claims are limited to cell-free extract. The Applicant has amended the claims to read on methods of rendering "a purified product isolated from blood or a biotechnologically produced product substantially free of lipid enveloped viruses." The Applicant has also, however, argued that the claims read on a method of "directly inactivating viruses in a cell-free biological product." As noted above, the claims have been amended to remove the claim language "cell-free." The Examiner therefore does not agree with the Applicant's interpretation of the claim language. The claims do not read so narrowly as

to exclude biologically produced products other than cells. In view of this, the rejection is maintained.

However, it is noted that there are several examples provided as to the types of products that may be rendered substantially virus free by the claimed method. See, App., pages 2 and 9. Many of these products are specific proteins, and also listed are recombinant and human proteins generally. In view of this, it is suggested that the claims be amended to read on the rendering of isolated proteins, rather than blood or biotechnologically produced products, substantially free of virus.

14. **(Prior Rejection- Withdrawn)** Claims 1-11, 13-15, 18, and 19 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As claim 19 has been cancelled from the application, the rejection is withdrawn as to this claim as moot. Prior to the amendment in the RCE, the claims read on "cell-free" biological products. The claims were amended in the RCE to describe the reduction of viral titer in composition of "a purified product isolated from blood or a biotechnologically produced product," rather than the rejected "cell-free" products. Because the specification does provide support for these terms, the rejection is withdrawn. However, it is noted that the specification does not define these terms as limited to cell-free products, or in other ways exclude cells from the products encompassed by these terms.

.Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. **(Prior Rejection-Reformed and Maintained)** Claims 1, 3-7, 9, 10, 14, 15, 18, and 19 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Itokawa et al., Chem Pharm Bull 42(3): 604-607. This rejection is hereby reformed such that those claims still pending in the application, 1, 3-7, 9, 10, 14, 15, and 18, are rejected as obvious over Itokawa in view of Budowsky et al, U.S. 6,114,108. These claims read on a method of reducing viral titer in a sample of a biotechnologically produced product comprising exposing the product to a disclosed lipoheptapeptide for a period of between 30 minutes to 2 hours at room temperature and at a concentration of 1-100 μM. As claim 19 has been cancelled from the application, the rejection is withdrawn as to this claim as moot.

The Itokawa reference teaches that surfactins isolated from B. subtilis demonstrate antiviral activities. Further, the reference also teaches that such activities are demonstrable where the surfactin concentration is 2 x 10-5 or 1.4 x 10-5 M. Page 607. These concentrations form a range (14 to 20 μM) that falls within the concentration used in the claimed method. However, Itokawa does not teach the use of the surfactins to render a composition of an isolated product substantially free of virus.

Budowsky teaches the use of compounds with anti-viral activity to inactivate virus in a composition such as blood plasma, or biopolymer (e.g. proteins) containing composition. Abstract, columns 3-4. In view of the teachings of the antiviral activities of the surfactins as described by Itokawa, it would have been obvious to one of ordinary skill in the art to have used the surfactins in the methods described by Budowsky.

In the RCE, the Applicant traversed the rejection over Itokawa on the grounds that it would not have been obvious to one of ordinary skill in the art that the compounds of Itokawa would have been so effective in the inactivation of viruses that the claimed method, wherein the contacting step lasts for a period of only 30 minutes to two hours. This argument is not found persuasive. As stated by the Examiner in the prior action, the time period of the contacting step would have been obvious to one of ordinary skill in the art as the optimization of a obvious method. Further, the greater efficacy of the compound than expected would, in this case, be a latent property of the claimed invention. See MPEP § 2145 II. This is because, as described above, the combined teachings of Itokawa and Budowsky render the claimed method obvious. The greater efficacy would, as stated by the Examiner in the prior action, be an inherent property of the method described by the prior art. For these reasons, and those of record in the prior actions, the rejection of the identified claims is maintained over the teachings of Itokawa and Budowsky.

17. **(Prior Rejection-Withdrawn)** Claims 1, 3, 9, and 10 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Naruse et al., J Antibiotics 43(3): 267-280 (March 1990). The claims have been described above. The Applicant has traversed this rejection

on the grounds that Naruse does not describe the lipopeptide disclosed in the present claims. The Examiner agrees that the teachings of Naruse alone do not suffice to maintain the rejection. The rejection is therefore withdrawn.

18. **(Prior Rejection-Withdrawn in part, Restated and Maintained in part)** Claims 2 and 13 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Itokawa or Naruse, in further view of Horowitz et al., Transfusion 25(6): 516-522. These claims describe the claimed method wherein the contacting is conducted at above room temperature (30-60 °C) for a period of 5-30 minutes. No additional traversal s to these rejections were made over those made against Itokawa and Naruse individually. In view of the above, the Examiner withdraws this rejection to the extent that it depends on Naruse, and maintains the rejection of claims 2 and 13 over Itokawa in view of Budowsky, and further in view of Horowitz.

19. **(Prior Rejection- Restated and Maintained in part)** Claims 8 and 11 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Itokawa, Naruse, and Vater et al., Proc 4th European Congress on Biotechnology 1987, Vol. 3, pages 266-269. The rejection of the claims is restated, and maintained, such that the claims are now rejected over the combined teachings of Itokawa, Naruse, Vaters as described on pages 11 and 12 of the rejection mailed on June 6, 2000, further in view of Budowsky as described above. Claims 8 and 11 further limit the lipopeptide of formula I to embodiments wherein the positions marked by X and Y are independently either Val or Ile (instead of Val, Ile, or Leu), and for claim 11, wherein the position marked by Z is Val (rather than Val or Ala). The rejection is maintained

for both the reasons of record, and because the references of Itokawa, Naruse, and Vaters each indicate that the structurally related lipopeptides, among which there are substantial sequence variations, isolated from Bacillus bacteria are effective as antiviral compounds. Although none of the references specifically teach the lipopeptides of claims 8 and 11, the Applicant has indicated that these lipopeptides are also isolated from Bacillus subtilis. Application, page 9, example 1. As such, it would have been obvious to those in the art to have used any of the structurally related lipopeptides (to those disclosed in Vaters) as antiviral agents. As the Applicant has disclosed that all of the surfactins of formula I may be so isolated, it would therefore have been obvious to use any of them as antiviral agents even though the amino acid composition of all of the lipopeptides had not yet been determined.

As the Applicant has not traversed the rejection of these claims except to the extent that it relies on the teachings of Naruse and Itokawa individually, the rejection is maintained. The traversal of the rejection over Itokawa was not found persuasive, and the fact that Naruse does not teach the specific lipopeptides claimed does not make the reference less relevant as applied in the current rejection.

Conclusion

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
May 12, 2003

JAMES HOUSEL 5/17/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600